

Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1.– 116. (cancelled)

117. (previously presented) A pharmaceutical dosage form which comprises (a) a first drug which comprises at least one morphine derivative having antitussive activity and (b) at least one second drug, wherein a plasma half-life of the at least one second drug differs from a plasma half-life of the first drug and wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.

118. (currently amended) The dosage form of claim 117, wherein the at least one morphine derivative comprises at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

119. (previously presented) The dosage form of claim 118, wherein the first drug comprises at least one of codeine phosphate, dihydrocodeine bitartrate and hydrocodone bitartrate.

P24615

120. (previously presented) The dosage form of claim 118, wherein the first drug comprises codeine phosphate.

121. (previously presented) The dosage form of claim 118, wherein the at least one second drug comprises at least one of a decongestant, expectorant, mucus thinning drug, and antihistamine.

122. (previously presented) The dosage form of claim 117, wherein the at least one second drug comprises a decongestant.

123. (previously presented) The dosage form of claim 122, wherein the second drug comprises at least one of phenylephrine, pseudoephedrine and pharmaceutically acceptable salts thereof.

124. (previously presented) The dosage form of claim 118, wherein the at least one second drug comprises an antihistamine.

125. (previously presented) The dosage form of claim 124, wherein the antihistamine comprises at least one of chlorpheniramine, promethazine, carbinoxamine and pharmaceutically acceptable salts thereof.

126. (previously presented) The dosage form of claim 117, wherein the at least one second drug comprises an expectorant.

127. (previously presented) The dosage form of claim 126, wherein the expectorant comprises guaifenesin.

128. (previously presented) The dosage form of claim 117, wherein the plasma half-life of the at least one second drug differs from the plasma half-life of the first drug by at least about 2 hours.

129. (previously presented) The dosage form of claim 118, wherein a plasma half-life of the at least one second drug differs from a plasma half-life of the first drug by at least about 3 hours.

130. (previously presented) The dosage form of claim 117, wherein a plasma half-life of the at least one second drug differs from a plasma half-life of the first drug by at least about 4 hours.

131. (previously presented) The dosage form of claim 128, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 80 % of the period of a plasma concentration within the therapeutic range of the first drug.

132. (previously presented) The dosage form of claim 117, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period of a plasma concentration within the therapeutic range of the first drug.

P24615

133. (previously presented) The dosage form of claim 130, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 95 % of the period of a plasma concentration within the therapeutic range of the first drug.

134. (previously presented) The dosage form of claim 117, wherein not more than about 30 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

135. (previously presented) The dosage form of claim 132, wherein not more than about 20 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

136. (previously presented) The dosage form of claim 131, wherein not more than about 10 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

137. (previously presented) The dosage form of claim 118, wherein the dosage form comprises a tablet.

138. (previously presented) The dosage form of claim 137, wherein the tablet is a bi-layered tablet.

139. (previously presented) The dosage form of claim 137, wherein the tablet comprises a matrix which comprises the first drug and has dispersed therein particles which comprise the at least one second drug.

140. (previously presented) A bi-layered tablet which comprises a first layer and a second layer, the first layer comprising a first drug which comprises at least one morphine derivative having antitussive activity, and the second layer comprising at least one second drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines, wherein the bi-layered tablet provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 80 % of a period over which the bi-layered tablet provides a plasma concentration within a therapeutic range of the first drug.

141. (previously presented) The dosage form of claim 140, wherein not more than about 20 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

142. (previously presented) The bi-layered tablet of claim 140, wherein the first layer

P24615

comprises at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

143. (previously presented) The bi-layered tablet of claim 142, wherein the second layer comprises at least one of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

144. (previously presented) The bi-layered tablet of claim 141, wherein the tablet comprises at least two of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

145. (previously presented) The bi-layered tablet of claim 140, wherein the first layer only comprises one or more of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof as active ingredient(s).

146. (previously presented) The bi-layered tablet of claim 140, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period of a plasma concentration within the therapeutic range of the first drug.

147. (previously presented) The bi-layered tablet of claim 140, wherein not more than about 10 % of a total period over which the plasma concentration of the at least one second drug is within

P24615

the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

148. (previously presented) The bi-layered tablet of claim 140, wherein at least one of the first and second layers is an immediate release layer.

149. (previously presented) The bi-layered tablet of claim 148, wherein the first layer is an immediate release layer.

150. (previously presented) The bi-layered tablet of claim 140, wherein both of the first and second layers are controlled release layers.

151. (previously presented) The bi-layered tablet of claim 149, wherein the first layer comprises a total of from about 0.1 mg to about 120 mg of at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

152. (previously presented) The bi-layered tablet of claim 140, wherein the first layer comprises a total of from about 5 mg to about 90 mg of at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

153. (previously presented) The bi-layered tablet of claim 151, wherein the first layer comprises a total of from about 25 mg to about 50 mg of at least one of codeine, dihydrocodeine,

hydrocodone and pharmaceutically acceptable salts thereof.

154. (previously presented) The bi-layered tablet of claim 152, wherein the second layer comprises at least one of (i) from about 0.1 mg to about 16 mg of chlorpheniramine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of chlorpheniramine; (ii) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; (iii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine; (iv) from about 0.1 mg to about 75 mg of promethazine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of promethazine; (v) from about 0.1 mg to about 32 mg of carbinoxamine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of carbinoxamine; and (vi) from about 1 mg to about 2400 mg of guaifenesin or an equivalent amount of at least one pharmaceutically acceptable salt of guaifenesin.

155. (previously presented) The bi-layered tablet of claim 140, wherein the tablet comprises at least one of (i) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; and (ii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine, and the second layer comprises at least one of an antihistamine and an expectorant.

156. (previously presented) The bi-layered tablet of claim 151, wherein not more than about 20 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

157. (previously presented) The bi-layered tablet of claim 152, wherein not more than about 10 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

158. (previously presented) The bi-layered tablet of claim 154, wherein not more than about 10 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

159. (previously presented) A pharmaceutical dosage form which comprises (a) a first drug which comprises at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof and has a first plasma half-life and (b) at least one second drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines and has a second plasma half-life which differs from the first plasma half-life by at least about 3 hours, wherein the dosage form provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 80 % of a period

P24615

over which the dosage form provides a plasma concentration within a therapeutic range of the first drug.

160. (previously presented) The dosage form of claim 159, wherein not more than about 10 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

161. (previously presented) The dosage form of claim 159, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period over which the dosage form provides a plasma concentration within the therapeutic range of the first drug.

162. (previously presented) The dosage form of claim 161, wherein not more than about 5 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

163. (previously presented) The dosage form of claim 159, wherein the dosage form comprises a multi-layered tablet.

164. (previously presented) The dosage form of claim 159, wherein the dosage form is

associated with instructions to administer the dosage form three or fewer times per day.

165. (previously presented) The dosage form of claim 117, wherein the dosage form is associated with instructions to administer the dosage form once or twice per day.

166. (previously presented) A pharmaceutical dosage form which comprises (a) at least one first morphine derivative in a first form or layer and (b) at least one second morphine derivative which is different from the first morphine derivative in a second form or layer which is different from the first form or layer, wherein the dosage form releases the at least one first morphine derivative at least one of over a different period and at a different rate than the at least one second morphine derivative.

167. (previously presented) The dosage form of claim 166, wherein the at least one first morphine derivative and the at least one second morphine derivative are independently selected from codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

168. (previously presented) The dosage form of claim 167, wherein the at least one first morphine derivative and the at least one second morphine derivative comprise at least one of codeine phosphate, dihydrocodeine bitartrate and hydrocodone bitartrate.

169. (previously presented) The dosage form of claim 166, wherein the dosage form comprises codeine phosphate.

P24615

170. (previously presented) The dosage form of claim 167, wherein the first form or layer is an immediate release form or layer and the second form or layer is a controlled release form or layer.

171. (previously presented) The dosage form of claim 166, wherein the dosage form is a bi-layered tablet which comprises an immediate release layer and a controlled release layer, which layers independently comprise at least one of codeine, dihydrocodeine, hydrocodone and pharmaceutically acceptable salts thereof.

172. (previously presented) The dosage form of claim 171, wherein the dosage form further comprises at least one additional drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines.

173. (previously presented) The dosage form of claim 171, wherein at least the immediate release layer thereof comprises the at least one additional drug.

174. (previously presented) The dosage form of claim 171, wherein at least the controlled release layer thereof comprises the at least one additional drug.

175. (previously presented) The dosage form of claim 166, wherein the dosage form releases the at least one first morphine derivative over a different period and at a different rate than the at least one second morphine derivative.

P24615

176. (previously presented) The dosage form of claim 175, wherein the dosage form releases the at least one first morphine derivative over a different period than the at least second morphine derivative.

177. (previously presented) The dosage form of claim 175, wherein the dosage form releases the at least one first morphine derivative over a first period and the at least one second morphine derivative over a second period and not more than about 30 % of the second period are coextensive with all or a part of the first period.

178. (previously presented) The dosage form of claim 177, wherein there is substantially no overlap between the first and second periods.

179. (previously presented) The dosage form of claim 166, wherein the dosage form releases the at least one first morphine derivative at a different rate than the at least second morphine derivative.

180. (previously presented) A bi-layered tablet which comprises a first layer and a second layer, the first layer comprising a first drug which is selected from codeine and pharmaceutically acceptable salts thereof, and the second layer comprising at least one second drug which is selected from decongestants, expectorants, mucus thinning drugs, and antihistamines, wherein the bi-layered tablet provides a plasma concentration within a therapeutic range of the at least one second drug over a period which is coextensive with at least about 70 % of a period over

P24615

which the bi-layered tablet provides a plasma concentration within a therapeutic range of the first drug.

181. (previously presented) The bi-layered tablet of claim 180, wherein the first layer comprises codeine phosphate.

182. (previously presented) The bi-layered tablet of claim 181, wherein the second layer comprises at least one of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

183. (previously presented) The bi-layered tablet of claim 181, wherein the tablet comprises at least two of phenylephrine, pseudoephedrine, chlorpheniramine, carbinoxamine, promethazine, guaifenesin and pharmaceutically acceptable salts thereof.

184. (previously presented) The bi-layered tablet of claim 180, wherein the first layer comprises only one or more of codeine and pharmaceutically acceptable salts thereof as active ingredient(s).

185. (previously presented) The bi-layered tablet of claim 180, wherein the period of a plasma concentration within the therapeutic range of the at least one second drug is coextensive with at least about 80 % of the period of a plasma concentration within the therapeutic range of the first drug.

186. (previously presented) The bi-layered tablet of claim 184, wherein the period of a plasma concentration within a therapeutic range of the at least one second drug is coextensive with at least about 90 % of the period of a plasma concentration within a therapeutic range of the first drug.

187. (previously presented) The bi-layered tablet of claim 180, wherein not more than about 20 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

188. (previously presented) The bi-layered tablet of claim 185, wherein not more than about 20 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

189. (previously presented) The bi-layered tablet of claim 186, wherein not more than about 10 % of a total period over which the plasma concentration of the at least one second drug is within the therapeutic range is outside the period over which the plasma concentration of the first drug is within the therapeutic range.

190. (previously presented) The bi-layered tablet of claim 180, wherein at least one of the first and second layers is an immediate release layer.

P24615

191. (currently amended) The bi-layered tablet of claim 494 190, wherein the first layer is an immediate release layer.

192. (previously presented) The bi-layered tablet of claim 190, wherein the second layer is an immediate release layer.

193. (previously presented) The bi-layered tablet of claim 180, wherein both of the first and second layers are controlled release layers.

194. (previously presented) The bi-layered tablet of claim 180, wherein the first layer comprises a total of from about 5 mg to about 90 mg of at least one of codeine and a pharmaceutically acceptable salt thereof.

195. (previously presented) The bi-layered tablet of claim 180, wherein the first layer comprises a total of from about 25 mg to about 50 mg of at least one of codeine phosphate.

196. (previously presented) The bi-layered tablet of claim 195, wherein the second layer comprises at least one of (i) from about 0.1 mg to about 16 mg of chlorpheniramine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of chlorpheniramine; (ii) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; (iii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other

pharmaceutically acceptable salt of pseudoephedrine; (iv) from about 0.1 mg to about 75 mg of promethazine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of promethazine; (v) from about 0.1 mg to about 32 mg of carbinoxamine maleate or an equivalent amount of at least one other pharmaceutically acceptable salt of carbinoxamine; and (vi) from about 1 mg to about 2400 mg of guaifenesin or an equivalent amount of at least one pharmaceutically acceptable salt of guaifenesin.

197. (previously presented) The bi-layered tablet of claim 195, wherein the first layer comprises at least one of (i) from about 1 mg to about 90 mg of phenylephrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of phenylephrine; and (ii) from about 1 mg to about 240 mg of pseudoephedrine hydrochloride or an equivalent amount of at least one other pharmaceutically acceptable salt of pseudoephedrine, and the second layer comprises at least one of an antihistamine and an expectorant.

198. (previously presented) The dosage form of claim 120, wherein the second drug comprises at least one drug selected from phenylephrine, pseudoephedrine and pharmaceutically acceptable salts thereof.

199. (previously presented) The dosage form of claim 120, wherein the at least one second drug comprises at least one drug selected from chlorpheniramine, promethazine, carbinoxamine and pharmaceutically acceptable salts thereof.

P24615

200. (previously presented) The dosage form of claim 120, wherein the at least one second drug comprises guaifenesin.